

DOCKET NO.: CEPH-0425

#3
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of:

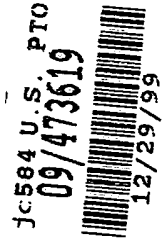
Robert Siman et al.

Serial No.: 08/967,625

Group No.: Not Yet Assigned

Filed: November 12, 1997

Examiner: Not Yet Assigned



For: **METHODS FOR DETECTING CELL APOPTOSIS**

I, Paul K. Legaard, Registration No. 38,534 certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

On

April 24, 1998
Paul K. Legaard
Paul K. Legaard Reg. No. 38,534

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 C.F.R. §1.56 and in accordance with 37 C.F.R. §§1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 C.F.R. §1.56(b).

(XX) In accordance with §1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in §1.491, or before the mailing date of a first Office Action on the merits of the above-identified application, no additional fee is required.

- () In accordance with §1.129(a), this Information Disclosure Statement is being filed in connection with () the first or () second After Final Submission, therefore:
 - (-) Certification in Accordance with §1.97(e) is attached; or
 - () The fee of \$240.00 as set forth in §1.17(p) is attached.
- () In accordance with §1.97(c), this Information Disclosure Statement is being filed after the period set forth in §1.97(b) above but before the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311, therefore:
 - () Certification in Accordance with §1.97(e) is attached; or
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- () In accordance with §1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311 but before the payment of the Issue Fee, therefore included are: Certification in Accordance with §1.97(e); Petition Requesting Consideration of the Information Disclosure Statement; and the fee of \$130.00 as set forth in §1.17(i)(1).
- (XX) Copies of each of the references listed on the attached Form PTO-1449 are enclosed herewith.
- () Copies of references listed on the attached Form PTO-1449 are enclosed herewith EXCEPT THAT:
 - () In view of the voluminous nature of references [list as appropriate], and the likelihood that these references are available to the Examiner, copies are not enclosed herewith.
 - () In accordance with §1.98(d), copies of the following references listed on the attached Form PTO-1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C. §120 have been made in the instant application:
 - () Copies of references [list as appropriate] listed on the attached Form PTO-1449 were previously cited by or submitted to the Patent and Trademark Office in prior application Serial No. , filed .

() If any of the foregoing publications are not available to the Examiner,
Applicant will endeavor to supply copies at the Examiner's request.

Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050.

This form is submitted in triplicate.

There are no listed references which are not in the English language.

Date:

April 24, 1998



Signature

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Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. CEPH-0425	Serial No. 08/967,625	JCS84 U.S. PTO 09/473619 12/29/99
		Applicant Robert Siman et al.		
		Filing Date November 12, 1997	Group Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)				
	AA	Alnenui et al., "Cloning and Expression of Four Novel Isoforms of Human Interleukin-1 β Converting Enzyme with Different Apoptotic Activities", <i>J. Biol. Chem.</i> , 1995, 270(9), 4312-4317		
	AB	Batistatou et al., "Bcl-2 Affects Survival but Not Neuronal Differentiation of PC12 Cells", <i>J. Neurosci.</i> , 1993, 13(10), 4422-4428		
	AC	Cherney et al., "cDNA sequence, protein structure, and chromosomal location of the human gene for poly(ADP-ribose) polymerase", <i>Proc. Natl. Acad. Sci. USA</i> , 1987, 84, 8370-8374		
	AD	Cohen et al., "Key morphological features of apoptosis may occur in the absence of internucleosomal DNA fragmentation", <i>Biochem. J.</i> , 1992, 286, 331-334		
	AE	Collins et al., "Continuous growth and differentiation of human myeloid leukaemic cells in suspension culture", <i>Nature</i> , 1977, 270, 347-349		
	AF	Crompton et al., "Propidium iodide staining correlates with the extent of DNA degradation in isolated nuclei", <i>Biochem. Biophys. Res. Commun.</i> , 1992, 183(2), 532-537		
	AG	Duan et al., "ICE-LAP6, a Novel Member of the ICE/Ced-3 Gene Family, Is Activated by the Cytotoxic T Cell Protease Granzyme B", <i>J. Biol. Chem.</i> , 1996, 271(28), 16720-16724		
	AH	Enari et al., "Sequential activation of ICE-like and CPP32-like proteases during Fas-mediated apoptosis", <i>Nature</i> , 1996, 380, 723-726		
	AI	Enari et al., "Involvement of an ICE-like protease in Fas-mediated apoptosis", <i>Nature</i> , 1995, 375, 78-81		
	AJ	Faucheu et al., "A novel human protease similar to the interleukin-1 β converting enzyme induces apoptosis in transfected cells", <i>EMBO J.</i> , 1995, 14(9), 1914-1922		
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	AK	Fernandes-Alnemri et al., "CPP32, a Novel Human Apoptotic Protein with Homology to <i>Caenorhabditis elegans</i> Cell Death Protein Ced-3 and Mammalian Interleukin-1 β -converting Enzyme", <i>J. Biol. Chem.</i> , 1994, 269(49), 30761-30764	
	AL	Fernandes-Alnemri et al., "Mch3, a Novel Human Apoptotic Cysteine Protease Highly Related to CCP32", <i>Cancer Res.</i> , 1995, 55, 6045-6052	
	AM	Fernandes-Alnemri et al., "Mch2, a New Member of the Apoptotic Ced-3/Ice Cysteine Protease Gene Family", <i>Cancer Res.</i> , 1995, 55, 2737-2742	
	AN	Frey, "Nucleic Acid Dyes for Detection of Apoptosis in Live Cells", <i>Cytometry</i> , 1995, 21, 265-274	
	AO	Gagliardini et al., "Prevention of Vertebrate Neuronal Death by the <i>crmA</i> Gene", <i>Science</i> , 1994, 263, 826-828	
	AP	Gavrieli et al., "Identification of Programmed Cell Death In Situ via Specific Labeling of Nuclear DNA Fragmentation", <i>J. Cell Biol.</i> , 1992, 119(3), 493-501	
	AQ	Gu et al., "Cleavage of Poly(ADP-ribose) Polymerase by Interleukin-1 β Converting Enzyme and Its Homologs TX and Nedd-2", <i>J. Biol. Chem.</i> , 1995, 270(32), 18715-18718	
	AR	Hoepfner et al., "Programmed cell death: from development to disease", <i>Biochim. Biophys. Acta</i> , 1966, 1242, 217-220	
	AS	Huppi et al., "Sequence and organization of the mouse poly (ADP-ribose) polymerase gene", <i>Nucl. Acids Res.</i> , 1989, 17(9), 3387-3401	
	AT	Ittel et al., "Chicken poly(ADP-ribose) synthetase: complete deduced amino acid sequence and comparison with mammalian enzyme sequences", <i>Gene</i> , 1991, 102, 157-164	
	AU	Kamens et al., "Identification and Characterization of ICH-2, a Novel Member of the Interleukin- β -converting Enzyme Family of Cysteine Proteases", <i>J. Biol. Chem.</i> , 1995, 270(25), 15250-15256	
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	AV	Kaufmann et al., "Specific Proteolytic Cleavage of Poly(ADP-ribose) Polymerase: An Early Marker of Chemotherapy-induced Apoptosis", <i>Cancer Res.</i> , 1993, 53, 3976-3985	
	AW	Lamarre et al., "Production and characterization of monoclonal antibodies specific for the functional domains of poly(ADP-ribose) polymerase", <i>Biochem. Cell Biol.</i> , 1986, 64, 368-376	
	AX	Lassmann et al., "Cell death in Alzheimer's disease evaluated by DNA fragmentation in situ", <i>Acta. Neuropathol.</i> , 1995, 89, 35-41	
	AY	Lazebnik et al., "Cleavage of poly(ADP-ribose) polymerase by a proteinase with properties like ICE", <i>Nature</i> , 1994, 371, 346-347	
	AZ	Lippke et al., "Identification and Characterization of CPP32/Mch2 Homolog 1, a Novel Cysteine Protease Similar to CPP32", <i>J. Biol. Chem.</i> , 1996, 271(4), 1825-1828	
	BA	Los et al., "Requirement of an ICE/CED-3 protease for Fas/APO-1-mediated apoptosis", <i>Nature</i> , 1995, 375, 81-83	
	BB	Malik et al., "Antibody to poly(adenosine diphosphate-ribose) polymerase and its use in chromatin analysis", <i>Nucl. Acid Res.</i> , 1982, 10(9), 2939-2950	
	BC	Martin et al., "Protease Activation during Apoptosis: Death by a Thousand Cuts?", <i>Cell</i> , 1995, 82, 349-352	
	BD	Meyer et al., "Enzymatic Properties of Recombinant ICH-1L Support a Role in Mediating Apoptosis", <i>Soc. Neurosci.</i> , 1996, 22, 565, Abstract No. 228.3	
	BE	Milligan et al., "Peptide Inhibitors of the ICE Protease Family Arrest Programmed Cell Death of Motoneurons In Vivo and Vitro", <i>Neuron</i> , 1995, 15, 385-393	
	BF	Miura et al., "Induction of Apoptosis in Fibroblasts by IL-1 β -Converting Enzyme, a Mammalian Homolog of the C. elegans Cell Death Gene <i>ced-3</i> ", <i>Cell</i> , 1993, 75, 653-660	
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		Filing Date November 12, 1997	Group Not Yet Assigned
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	BG	Muzio et al., "FLICE, A Novel FADD-Homologous ICE/CED-3-like Protease, is Recruited to the CD95 (Fas/APO-1) Death-Inducing Signaling Complex", <i>Cell</i> , 1996, 85, 817-827	
	BH	Nicholson et al., "Identification and inhibition of the ICE/CED-3 protease necessary for mammalian apoptosis", <i>Nature</i> , 1995, 376, 37-43	
	BI	Nicoletti et al., "A rapid and simple method for measuring thymocyte apoptosis by propidium iodide staining and flow cytometry", <i>J. Immunol. Methods</i> , 1991, 139, 271-279	
	BJ	Nitatori et al., "Delayed Neuronal Death in the CA1 Pyramidal Cell Layer of the Gerbil Hippocampus following Transient Ischemia is Apoptosis", <i>J. Neurosci.</i> , 1995, 15(2), 1001-1011	
	BK	Oppenheim, "Cell Death During Development of the Nervous System", <i>Annu. Rev. Neurosci.</i> , 1991, 14, 453-501	
	BL	Roberts-Lewis et al., "Immunolocalization of Calpain I-mediated Spectrin Degradation to Vulnerable Neurons in the Ischemic Gerbil Brain", <i>J. Neurosci.</i> , 1994, 14(6), 3934-3944	
	BM	Saito et al., "Cloning of a full-length cDNA encoding bovine thymus poly(ADP-ribose) synthetase: evolutionarily conserved segments and their potential functions", <i>Gene</i> , 1990, 90, 249-254	
	BN	Schlegel et al., "CPP32/Apopain Is a Key Interleukin 1 β Converting Enzyme-like Protease Involved in Fas-mediated Apoptosis", <i>J. Biol. Chem.</i> , 1996, 271(4), 1841-1844	
	BO	Schulze-Osthoff et al., "Cell Nucleus and DNA Fragmentation Are Not Required for Apoptosis", <i>J. Cell Biol.</i> , 1994, 127(1), 15-20	
	BP	Shah et al., "Detection of Poly(ADP-Ribose) Polymerase and Its Apoptosis-Specific Fragment by a Nonisotopic Activity-Western Blot Technique", <i>Analyt. Biochem.</i> , 1995, 232, 251-254	
	BQ	Tewari et al., "Yama/CPP32 β , a Mammalian Homolog of CED-3, Is a CrmA-Inhibitable Protease That Cleaves the Death Substrate Poly(ADP-Ribose) Polymerase", <i>Cell</i> , 1995, 81, 801-809	
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	BR	Thompson, "Apoptosis in the Pathogenesis and Treatment of Disease", <i>Science</i> , 1995, 267, 1456-1462	
	BS	Troy et al., "The contrasting roles of ICE family proteases and interleukin-1 β in apoptosis induced by trophic factor withdrawal and by copper/zinc superoxide dismutase down-regulation", <i>Proc. Natl. Acad. Sci. USA</i> , 1996, 93, 5635-5640	
	BT	Wang et al., "Ich-1, an Ice/ced-3-Related Gene, Encodes Both Positive and Negative Regulators of Programmed Cell Death", <i>Cell</i> , 1994, 78, 739-750	
	BU	Wijsman et al., "A New Method to Detect Apoptosis in Paraffin Sections: In Situ End-labeling of Fragmented DNA", <i>J. Histochem. Cytochem.</i> , 1993, 41(1), 7-12	
	BV	Woo, "Apoptosis and Loss of Renal Tissue in Polycystic Kidney Diseases", <i>N. Engl. J. Med.</i> , 1995, 333, 18-25	
	BW	Wood et al., "In Situ Labeling of Granule Cells for Apoptosis-Associated DNA Fragmentation Reveals Different Mechanisms of Cell Loss in Developing Cerebellum", <i>Neuron</i> , 1993, 11, 621-632	
	BX	Wyllie, "Glucocorticoid-induced thymocyte apoptosis is associated with endogenous endonuclease activation", <i>Nature</i> , 1980, 284, 555-556	
	BY	Wyllie et al., "Chromatin Cleavage in Apoptosis: Association with Condensed Chromatin Morphology and Dependence on Macromolecular Synthesis", <i>J. Pathol.</i> , 1984, 142, 67-77	
	BZ	Zhivotovsky et al., "Multiple Proteases are Involved in Thymocyte Apoptosis", <i>Exp. Cell Res.</i> , 1995, 221, 404-412	
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U. S. PATENT DOCUMENTS							
Examiner Initial		Document No.	Date	Name	Class	Subclass	
	CA	5,536,639	07/16/96	Siman et al.	435	7.1	
	CB	5,605,826	02/25/97	Wright et al.	435	226	
FOREIGN PATENT DOCUMENTS							
Examiner Initial		Document No.	Date	Country	Translation YES NO		
EXAMINER				DATE CONSIDERED			